

Posters

6. Microbiology

S63

64 The prevalence of cochlear and vestibular dysfunction in patients with cystic fibrosis

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Objectives: The primary objective was to determine the prevalence of cochlear (C-DF) and vestibular (V-DF) dysfunction in patients with CF at LHSC. Secondary objectives included determining if there is an association between aminoglycoside (AMG) exposure or other risk factors and ototoxicity in CF patients.

Methods: 73 patients with C-DF and V-DF are needed to detect a 0–10% prevalence rate with 95% confidence. Patients with a diagnosis of CF were eligible for study enrollment. Study participants completed audiometric testing to detect C-DF. V-DF was detected by completing five standard balance tests. Additional risk factors for ototoxicity, including AMG exposure, were investigated.

Results: 49 patients (1–48 years of age) completed audiometric testing and 37 patients completed balance testing. Of these, 4 (8.9%) patients had C-DF and 20 (54.1%) patients had V-DF. There was no statistically significant difference in the rate of C-DF and V-DF in patients exposed to AMG as compared to those not exposed (C-DF, $P=0.812$; V-DF, $P=0.051$). Family history of hearing loss, prematurity, loud noise exposure, or ototoxic medication use did not produce statistically significant higher rates of C-DF and V-DF.

Conclusion: The prevalence of C-DF and V-DF amongst CF patients at LHSC appears to be 8.9% (95% CI 3.5–20.7%) and 54.1% (95% CI 38.4–69.0%) respectively. The high rate of V-DF may be the result of physiological immaturity or acute illness, as opposed to a pathological process. AMG exposure does not appear to be associated with an increase in C-DF and V-DF rates amongst study participants and no other risk factors were identified which may predispose CF patients to ototoxicity.

66 Association of urinary kidney injury molecule-1 with aminoglycoside exposure in children with cystic fibrosis

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Objectives: Aminoglycoside antibiotics, commonly used for the treatment of pulmonary exacerbations in cystic fibrosis, are potentially toxic to renal proximal tubule epithelial cells. A novel urinary biomarker, Kidney Injury Molecule-1 (KIM-1), has specificity for proximal tubule injury. The aim of this study was to assess KIM-1 as a biomarker of aminoglycoside-induced nephrotoxicity in children with cystic fibrosis.

Methods: Baseline urine samples were collected from 44 children aged 0–16 years with cystic fibrosis, and before, during and after exposure to tobramycin in 10 of these children. KIM-1 was measured using a Meso Scale Discovery analytical platform, and standardised to urinary creatinine.

Results: Mean baseline KIM-1 was 0.57 ng/mg Cr (95% Confidence Interval (CI), 0.40–0.73 ng/mg Cr, $n=44$). There was a significant correlation between baseline KIM-1 and the number of previous courses of aminoglycosides ($R=0.70$, $P<0.002$). During exposure to tobramycin mean peak KIM-1 was significantly elevated from baseline (mean peak KIM-1, 1.24 ng/mg Cr, 95% CI, 0.71–1.78 ng/mg Cr, $p=0.02$, $n=10$). Mean fold change [(peak KIM-1 during tobramycin exposure)/(pre-treatment baseline KIM-1)] was 3.03 (95% CI, 1.89–4.17).

Conclusion: In children with cystic fibrosis we have demonstrated significant acute changes in urinary KIM-1 during exposure to tobramycin, and an association of baseline KIM-1 with previous aminoglycoside exposure. KIM-1 may be a useful, non-invasive, biomarker of acute and chronic proximal tubular injury associated with exposure to aminoglycosides in children with cystic fibrosis.

67 Relative Resistance Index – a scoring system for antibiotic resistance in *Pseudomonas aeruginosa*

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Objectives: There is a need to measure antibiotic resistance of *Pseudomonas aeruginosa* (PA) in cystic fibrosis (CF), either qualitatively or quantitatively, to inform patient management. The aim of this study was to develop a simple method by which resistance can be quantified by calculating a relative resistance index (RRI), and to assess correlation of RRIs with clinical variables.

Methods: In our model, RRIs were calculated based on resistance to aztreonam, ceftazidime, ciprofloxacin, colistin, meropenem, tazocin, temicillin and tobramycin. Eighty-five adults with CF and chronic PA colonisation were identified. For each, all PA cultures between 2010–2011 were allocated a score of 0 for susceptible, 0.5 for intermediate resistance or 1 for resistant for each antibiotic listed above, and the RRI calculated by dividing the sum of these by the number of antibiotics. The mean RRIs for all cultures over 2010–2011 were correlated with clinical variables (including age, FEV₁, IV antibiotic days and BMI).

Results: RRIs for non-mucoid PA exhibited significant positive correlation with total number of IV days ($r=0.405$; $p<0.001$) and significant negative correlation with FEV₁ % predicted ($r=-0.437$ $p<0.001$). RRIs were not significantly correlated with duration of colonisation, typing (clonal vs other strain) or BMI. Median RRIs were significantly higher for females than males (0.26 vs. 0.14; $p=0.03$) for non-mucoid PA only. Meropenem resistance displayed the strongest negative correlation with FEV₁ % predicted.

Conclusion: In summary, RRI is an easily calculated measure which appears to have clinical significance, and enables quantitative monitoring of resistance over time.

68 Fast and convenient metalloprotease activity assay based on flow cytometry and its application in cystic fibrosis

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Objectives: *Pseudomonas aeruginosa* (Pa) is the most common pathogen of cystic fibrosis (CF). We focused on Pa metalloproteases (MP). The modulation of Pa virulence factors such as MPs was suggested as mechanism for azithromycin (AZM) beneficial effects in CF patients. Our work aimed to develop a highly reproducible and easy method to detect MP activity in Pa clinical strains and establish the sensitivity of it to AZM.

Methods: Fluorochrome-labeled substrate (FITC-gelatin) coated microspheres allowed to evaluate MP activity in conditioned media (CM) from Pa clinical strains and in sputa of CF patients and the effect of AZM treatment on Pa strains able to release MPs.

Results: MP activity was measured in CM from 136 isolates classified as sporadic and 134 defined as chronic. Activity was detected in 100 of 136 sporadic strains (73%) while this was true only for 70 of 134 (52%) chronic strains ($p<0.0001$, Fisher's exact test). AZM treatment induced decrease of MP activity in 76 of 91 (83%) sporadic strains while it had a similar effect only on 28 of 56 chronic strains (50%) ($p<0.0001$, Fisher's exact test). We measured MP activity in the cell-free sputa from CF patients Pa chronically colonized being untreated or treated with AZM ($n=37$). A strong decrease of fluorescence was detected in both conditions (76.4% reduction average based on MFI values, for $n=14$ untreated patients, 74.9% reduction for $n=23$ AZM-treated patients).

Conclusion: This method is sensitive and reproducible and allows a simple data interpretation. AZM treatment decrease MP activity in Pa. Bacterial MP released by Pa might contribute, along with leukocyte-derived enzymes, to lung damage in CF patients.